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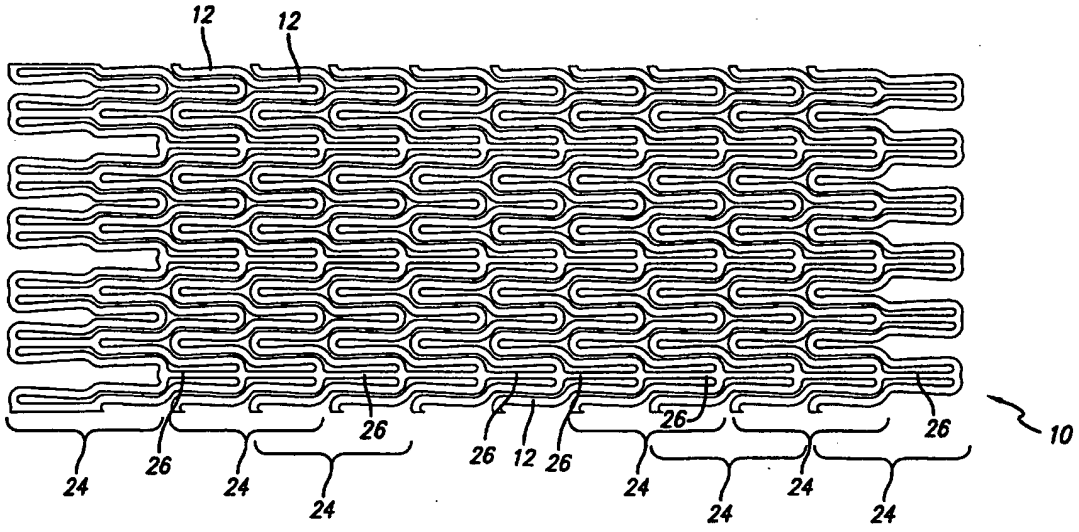
(54) Title: RADIOPAQUE NITINOL ALLOYS FOR MEDICAL DEVICES



(57) Abstract: A radiopaque nitinol medical device such as a stent for use with or implantation in a body lumen is disclosed. The stent is made from a superelastic alloy such as nickel-titanium or nitinol, and includes a ternary element selected from the group of chemical elements consisting of iridium, platinum, gold, rhenium, tungsten, palladium, rhodium, tantalum, silver, ruthenium, or hafnium. The added ternary element improves the radiopacity of the nitinol stent comparable to that of a stainless steel stent of the same size and strut pattern coated with a thin layer of gold. The nitinol stent has improved radiopacity yet retains its superelastic and shape memory behavior and further maintains a thin strut/wall thickness for high flexibility.

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Stents are widely used throughout the United States and in Europe and other countries. Generally speaking, the stents can take numerous forms. One of the most common is a generally cylindrical, hollow tube that holds open the vascular wall at the area that has been dilated by a dilation catheter. One highly regarded stent used and sold in the United States is known under the tradename ACS Multi-Link Stent, which is made by Advanced Cardiovascular Systems, Inc., Santa Clara, California.

In expandable stents that are delivered with expandable catheters, such as balloon catheters, the stents are positioned over the balloon portion of the catheter and are expanded from a reduced diameter to an enlarged diameter greater than or equal to the inner diameter of the arterial wall by inflating the balloon. Stents of this type can be expanded to an enlarged diameter by deforming the stent, by engagement of the stent walls with respect to one another, and by one way engagement of the stent walls together with endothelial growth onto and over the stent.

Examples of intravascular stents can be found in U.S. Patent No. 5,292,331 (Boneau); U.S. Patent No. 4,580,568 (Gianturco); U.S. Patent No. 4,856,516 (Hillstead); U.S. Patent No. 5,092,877 (Pinchuk); and U.S. Patent No. 5,514,154 (Lau et al.), which are incorporated herein by reference in their entirety.

The problem with some prior art stents, especially those of the balloon expandable type, is that they are often stiff and inflexible. These balloon expandable type stents are commonly formed from stainless steel alloys and the stents are constructed so that they are expanded beyond their elastic limit. As a result, such stents are permanently deformed by the inflation balloon beyond their elastic limits to hold open a body lumen and thus maintain patency of that body lumen. There are several commercially available balloon expandable stents that are widely used; they are generally implanted in the coronary arteries after a PTCA procedure mentioned earlier.

Stents are often times implanted in vessels that are closer to the surface of the body, such as in the carotid arteries in the neck or in peripheral arteries and veins in the leg. Because these stents are so close to the surface of the body, they are particularly vulnerable to impact forces that can partially or completely collapse the

is the fact that they are not sufficiently radiopaque as compared to a comparable structure made from gold or tantalum. For example, radiopacity permits the cardiologist or physician to visualize the procedure involving the stent through use of fluoroscopes or similar radiological equipment. Good radiopacity is therefore a useful feature for self-expanding nickel-titanium stents to have.

Radiopacity can be improved by increasing the strut thickness of the nickel-titanium stent. But increasing strut thickness detrimentally affects the flexibility of the stent, which is a quality necessary for ease of delivery. Another complication is that radiopacity and radial force co-vary with strut thickness. Also, nickel-titanium is difficult to machine and thick struts exacerbates the problem.

Radiopacity can be improved through coating processes such as sputtering, plating, or co-drawing gold or similar heavy metals onto the stent. These processes, however, create complications such as material compatibility, galvanic corrosion, high manufacturing cost, coating adhesion or delamination, biocompatibility, loss of coating integrity following collapse and deployment of the stent, etc.

Radiopacity can also be improved by alloy addition. One specific approach is to alloy the nickel-titanium with a ternary element. What has been needed and heretofore unavailable in the prior art is a superelastic nickel-titanium stent that includes a ternary element to increase radiopacity yet preserves the superelastic qualities of the nitinol.

SUMMARY OF THE INVENTION

The present invention relates to a radiopaque medical device, such as a stent, for use or implantation in a body lumen. In a preferred embodiment, a radiopaque medical device, such as a stent, is constructed from a tubular-shaped body having a thin wall defining a strut pattern; wherein the tubular body includes a superelastic, nickel-titanium alloy, and the alloy further includes a ternary element selected from the group of chemical elements consisting of iridium, platinum, gold, rhenium, tungsten, palladium, rhodium, tantalum, silver, ruthenium, or hafnium. In a

wherein the stent is highly radiopaque. The step of providing a tubular-shaped body includes melting nickel, titanium, and the ternary element and cooling the mixture to form an alloy ingot, hot forming the alloy ingot, hot or cold forming the alloy ingot into a cylinder, drilling the cylinder to form tubing, cold drawing the tubing, and annealing the tubing.

The present invention of course envisions the minor addition of a quaternary element, for example, iron, to further enhance the alloy's formability or its thermomechanical properties. In short, the presence of elements in addition to the ternary elements cited above is contemplated.

In a preferred embodiment, an austenite finish temperature (A_f) of the superelastic alloy in the stent is greater than or equal to zero and less than or equal to 37 degrees C. Also in the preferred embodiment, the ingot after melting includes an austenite finish temperature (A_f) of greater than or equal to 0 degrees C and less than or equal to 40 degrees C. The tubing includes an austenite finish temperature (A_f) of greater than or equal to -15 degrees C and less than or equal to 15 degrees C.

Other features and advantages of the present invention will become more apparent from the following detailed description of the invention when taken in conjunction with the accompanying exemplary drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a side elevational view, partially in section, depicting a stent mounted on a delivery catheter and expanded within a damaged vessel, pressing a damaged vessel lining against the vessel wall.

FIG. 2 is a side elevational view, partially in section, depicting an expanded stent within the vessel after withdrawal of the delivery catheter.

FIG. 3 is an idealized stress-strain hysteresis curve for a superelastic material.

FIG. 4 is a plan view of the flattened strut pattern of an exemplary embodiment superelastic stent.

be nested. This strut pattern is best seen from the flattened plan view of FIG. 4. The serpentine patterned struts 12 are nested such that the extended portions of the struts of one cylindrical element 24 intrude into a complementary space within the circumference of an adjacent cylindrical element. In this manner, the plurality of cylindrical elements 24 can be more tightly packed lengthwise.

As introduced above, an exemplary stent of the present invention includes a superelastic material. In a general sense, superelasticity implies that the material can undergo a large degree of reversible strain as compared to common steel. In a technical sense, the term "superelasticity" and sometimes "pseudoelasticity" refer to an isothermal transformation in nitinol. More specifically, it refers to stress inducing a martensitic phase from an austenitic phase. Alloys having superelastic properties generally have at least two phases: a martensitic phase, which has a relatively low tensile strength and which is stable at relatively low temperatures, and an austenitic phase, which has a relatively high tensile strength and which is stable at temperatures higher than the martensitic phase. Superelastic characteristics generally allow the metal stent to be deformed by collapsing the stent and creating stress which causes the NiTi to reversibly change to the martensitic phase. The stent is restrained in the deformed condition inside a delivery sheath typically to facilitate the insertion into a patient's body, with such deformation causing the isothermal phase transformation. Once within the body lumen, the restraint on the stent is removed, thereby reducing the stress thereon so that the superelastic stent returns towards its original undeformed shape through isothermal transformation back to the austenitic phase. Under these conditions, the stent can be described as self-expanding.

Returning to FIG. 1, the graphic illustrates, in a partial cross-sectional view, the distal end of a rapid exchange stent delivery system that includes a guide wire 14, a delivery sheath 16, and an intravascular catheter 18. For the sake of clarity, the illustration of the delivery system in FIG. 1 has been simplified. It is just one example of a delivery system that may be used with the present invention. More details of a delivery system specifically for use with a self-expanding stent may be found in, for

body temperature.

According to theory, when stress is applied to a specimen of a metal such as nitinol exhibiting superelastic characteristics at a temperature at or above that which the transformation of the martensitic phase to the austenitic phase is complete, the specimen deforms elastically until it reaches a particular stress level where the alloy then undergoes a stress-induced phase transformation from the austenitic phase to the martensitic phase. As the phase transformation progresses, the alloy undergoes significant increases in strain with little or no corresponding increases in stress. The strain increases while the stress remains essentially constant until the transformation of the austenitic phase to the martensitic phase is complete. Thereafter, further increase in stress is necessary to cause further deformation. The martensitic metal first yields elastically upon the application of additional stress and then plastically with permanent residual deformation.

If the load on the specimen is removed before any permanent deformation has occurred, the stress-induced martensite elastically recovers and transforms back to the austenitic phase. The reduction in stress first causes a decrease in strain. As stress reduction reaches the level at which the martensitic phase begins to transform back into the austenitic phase, the stress level in the specimen remains essentially constant (but less than the constant stress level at which the austenitic crystalline structure transforms to the martensitic crystalline structure until the transformation back to the austenitic phase is complete); i.e., there is significant recovery in strain with only negligible corresponding stress reduction. After the transformation back to austenite is complete, further stress reduction results in elastic strain reduction. This ability to incur significant strain at relatively constant stress upon the application of a load and to recover from the deformation upon the removal of the load is commonly referred to as "superelasticity" and sometimes "pseudoelasticity."

FIG. 3 illustrates an idealized stress-strain hysteresis curve for a superelastic, binary nickel-titanium alloy. The relationship is plotted on x-y axes, with the x axis representing strain and the y axis representing stress. For ease of illustration,

emphasized above, the superelastic curve is characterized by regions of nearly constant stress upon loading, identified above as loading plateau stress C-D and unloading plateau stress G-H. Naturally, the loading plateau stress C-D always has a greater magnitude than the unloading plateau stress G-H. The loading plateau stress represents the period during which martensite is being stress-induced in favor of the original austenitic crystalline structure. As the load is removed, the stress-induced martensite transforms back into austenite along the unloading plateau stress part of the curve. The difference in stress between the stress at loading C-D and unloading stress G-H defines the hysteresis of the system.

The present invention seeks to preserve the superelastic qualities of nickel-titanium alloys just described yet improve upon the material's radiopacity by addition of a ternary element. This is preferably accomplished in one embodiment by forming a composition consisting essentially of about 30 to about 52 percent titanium and the balance nickel and up to 10 percent of one or more additional ternary alloying elements. Such ternary alloying elements may be selected from the group consisting of iridium, platinum, gold, rhenium, tungsten, palladium, rhodium, tantalum, silver, ruthenium, or hafnium. In the preferred embodiment, the atomic percentage of platinum is greater than or equal to 2.5 and less than or equal to 15. In an alternative embodiment, the atomic percentage of palladium is greater than or equal to 2.5 and less than or equal to 20.

A preferred embodiment stent according to the present invention has 42.8 atomic percent nickel, 49.7 atomic percent titanium, and 7.5 atomic percent platinum. Through empirical studies, the aforementioned compositions produce stent patterns having a radiopacity comparable to the same size and pattern stent made from 316 L stainless steel with a 2.7 to 6.5 μm gold coating.

In various alternative embodiments, the present invention contemplates the minor addition of a quaternary element, for example, iron, to further enhance the alloy's formability or its thermomechanical properties. The presence of impurities such as carbon or oxygen or the like in the present invention alloy is also possible.

Scanning Calorimeter (DSC) test, known in the art. The DSC test method to determine transformation temperatures for the ingot is guided by ASTM standard no. F 2004-00, entitled "Standard Test Method For Transformation Temperature Of Nickel-Titanium Alloys By Thermal Analysis."

The "active A_f" for the tubing and the finished stent is determined by a bend and free recovery test, also known in the art. In such a test, the tubing is cooled to under the M_f temperature, deformed, and warmed up. While monitoring the increasing temperature, the point of final recovery of the deformation in the tubing approximates the A_f of the material. The active A_f testing technique is guided by a second ASTM standard entitled "Standard Test Method For Determination Of Transformation Temperature Of Nickel-Titanium Shape Memory Alloys By Bend And Free Recovery," or by equivalent test methods known in the art.

Samples of wire made in accordance with the foregoing exemplary embodiments were tested. Specifically, the stress-strain relationship based on empirical data for nickel-titanium-palladium and nickel-titanium-platinum are plotted against binary nitinol in FIG. 5. Curve A corresponds to a sample of nickel-titanium-platinum. Curve B is based on a sample of binary nitinol. Curve C is based on a sample of nickel-titanium-palladium. To generate the empirical data, the wire samples were placed under increasing tension until past the phase transformation from their initial austenitic phase to their martensitic phase. Tension was then slowly released prior to any plastic deformation until stress on the samples dropped to zero with full deformation recovery.

As is apparent from the plot of FIG. 5, the present invention nickel-titanium-palladium and nickel-titanium-platinum alloys have stress-strain curves that closely follow the hysteresis curve for binary nitinol. All three curves have essentially flat loading and unloading plateau stresses indicating the presence of a phase transformation that is characteristic of superelastic metals. Hence, the present invention nitinol stent incorporates a ternary element, in these exemplary embodiments palladium or platinum, to improve radiopacity yet the materials' superelastic capability

that the structure returns to its original, set shape. Nitinol alloys having shape memory effect generally have at least two phases: a martensitic phase, which has a relatively low tensile strength and which is stable at relatively low temperatures, and an austenitic phase, which has a relatively high tensile strength and which is stable at temperatures higher than the martensitic phase.

Shape memory effect is imparted to the alloy by heating the nickel-titanium metal to a temperature above which the transformation from the martensitic phase to the austenitic phase is complete; i.e., a temperature above which the austenitic phase is stable. The shape of the metal during this heat treatment is the shape "remembered." The heat-treated metal is cooled to a temperature at which the martensitic phase is stable, causing the austenitic phase to transform to the martensitic phase. The metal in the martensitic phase is then plastically deformed, e.g., to facilitate the entry thereof into a patient's body. Subsequent heating of the deformed martensitic phase to a temperature above the martensite to austenite transformation temperature causes the deformed martensitic phase to transform to the austenitic phase. During this phase transformation the metal reverts back towards its original shape.

The recovery or transition temperature may be altered by making minor variations in the composition of the metal and in processing the material. In developing the correct composition, biological temperature compatibility must be determined in order to select the correct transition temperature. In other words, when the stent is heated, it must not be so hot that it is incompatible with the surrounding body tissue. Other shape memory materials may also be utilized, such as, but not limited to, irradiated memory polymers such as autocrosslinkable high density polyethylene (HDPEX). Shape memory alloys are known in the art and are discussed in, for example, "Shape Memory Alloys," Scientific American, Vol. 281, pp. 74-82 (November 1979), incorporated herein by reference.

Shape memory alloys undergo a transition between an austenitic phase and a martensitic phase at certain temperatures. When they are deformed while in the martensitic phase, they retain this deformation as long as they remain in the same

present invention can be used in other instances. Other modifications and improvements may be made without departing from the scope of the present invention.

10. A superelastic, radiopaque metallic stent for medical applications, comprising:

a tubular-shaped body having a thin wall defining a strut pattern;

wherein the body includes a superelastic nickel-titanium alloy and the alloy further includes a third element selected from the group of chemical elements consisting of: iridium, platinum, gold, rhenium, tungsten, palladium, rhodium, tantalum, silver, ruthenium, or hafnium; and

wherein the stent exhibits a level of radiopacity.

11. The superelastic, radiopaque metallic stent of claim 10, wherein the radiopacity of the stent is substantially equivalent to a 316L stainless steel stent having an identical strut pattern and size and coated with 2.7 to 6.5 μm of gold.

12. The superelastic, radiopaque metallic stent of claim 10, wherein the atomic percent of platinum is greater than or equal to 2.5 and less than or equal to 15.

13. The superelastic, radiopaque metallic stent of claim 10, wherein the atomic percent of palladium is greater than or equal to 2.5 and less than or equal to 20.

14. The superelastic, radiopaque metallic stent of claim 10, wherein the thin wall is at least 10 percent thinner than an identically strut patterned stent having a substantially equivalent level of radiopacity.

15. The superelastic, radiopaque metallic stent of claim 10, wherein the strut pattern is laser cut from a tube.

16. A method for providing a superelastic, radiopaque metallic stent for medical applications, comprising:

providing a tubular-shaped body having a thin wall, wherein the body includes a superelastic nickel-titanium alloy and the alloy further includes a ternary element selected from the group of chemical elements consisting of: iridium, platinum, gold, rhenium, tungsten, palladium, rhodium, tantalum, silver, ruthenium, or hafnium;

forming a strut pattern;

wherein the stent is radiopaque.

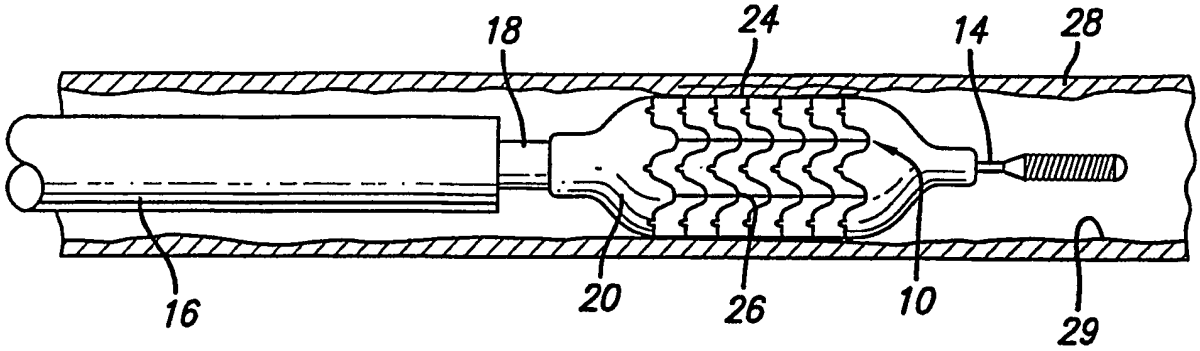


FIG. 1

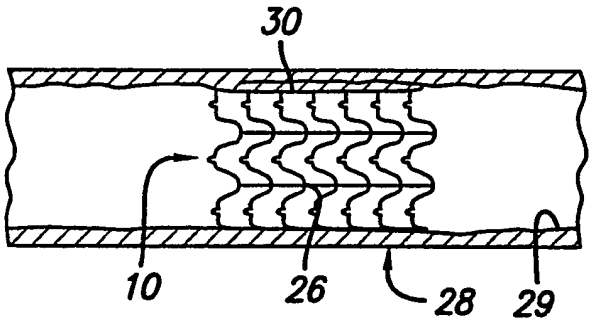


FIG. 2

FIG. 3

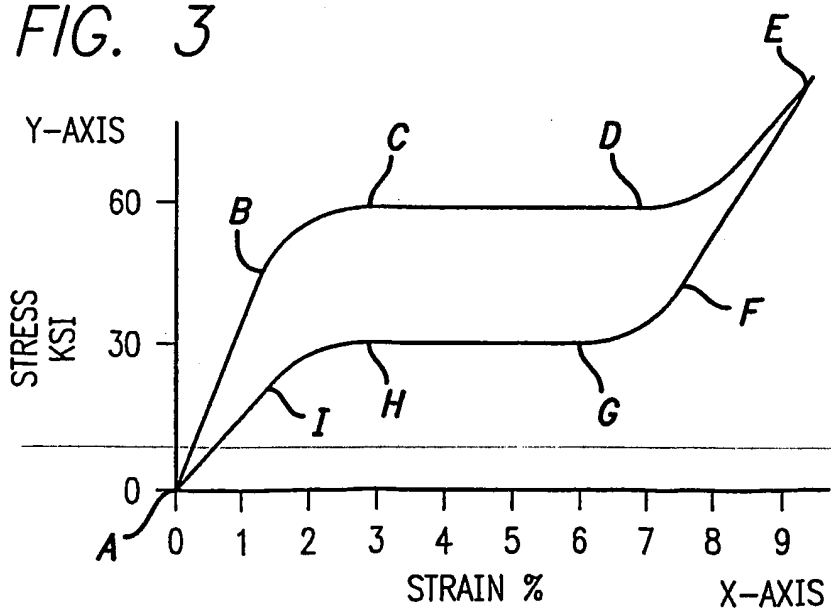
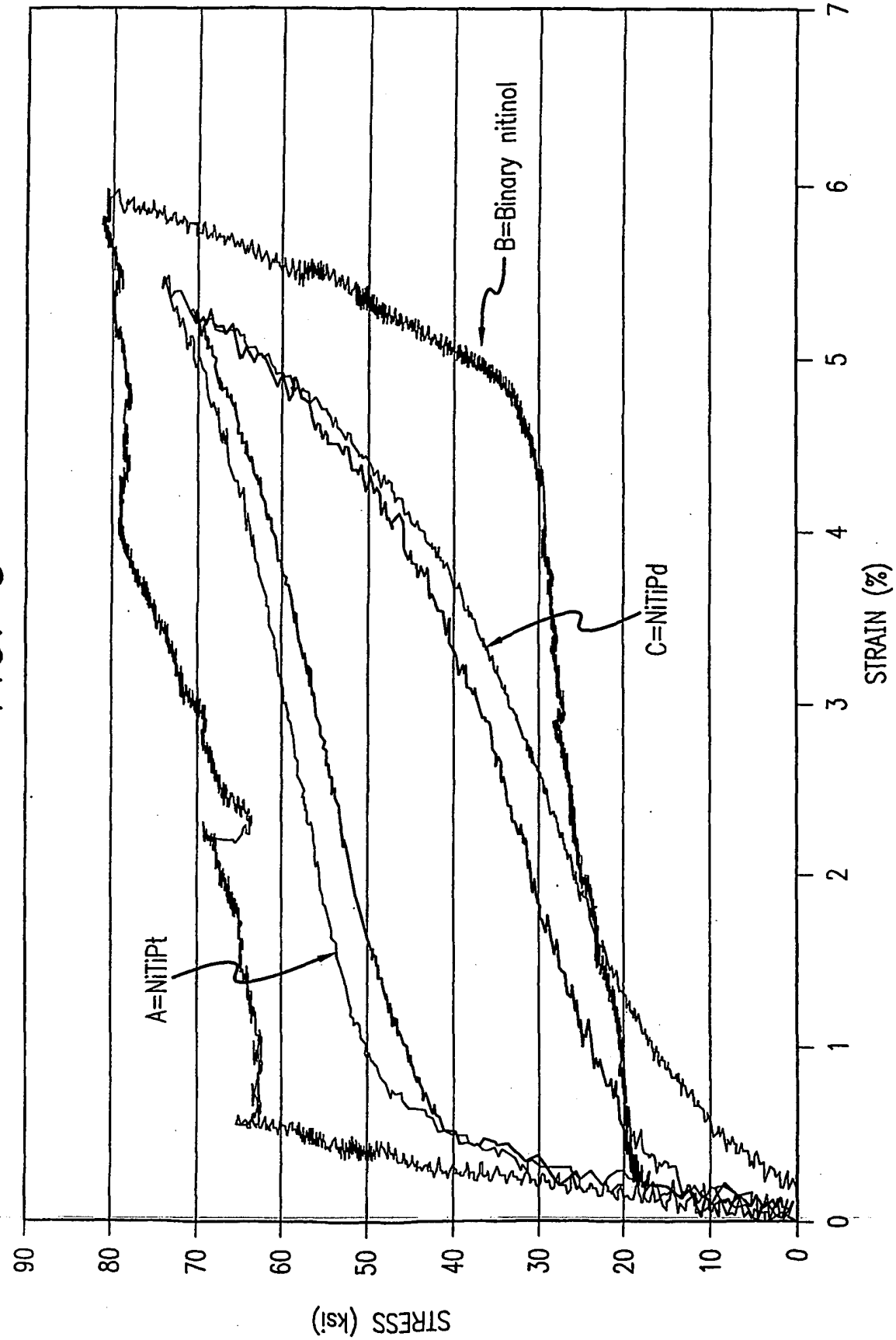


FIG. 5


B=Binary nitinol
C=NiTiPd
A=NiTiPt
STRESS (ksi)
STRAIN (%)
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7

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